Assessment of prenatal exposure to persistent organohalogen compounds from cord blood serum analysis in two Mediterranean populations (Valencia and Menorca)

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Abstract

Prenatal levels of organohalogen compounds (OHCs), including polybromodiphenyl ethers (PBDEs), polychlorobiphenyls (PCBs), hexachlorobenzene (HCB), hexachlorocyclohexanes and DDTs have been investigated in two different cohorts from the Spanish Mediterranean area, Valencia and Menorca, by analysis of cord blood serum. Comparison of the observed median concentrations to other cohorts show low PBDE levels (2.8-6.8 ng/g lipid) but high values of HCB (0.68 ng/ml, 260 ng/g lipid) and PCBs (0.65 ng/ml, 240 ng/g lipid) in the cohort of Menorca indicating that Mediterranean areas, and not only high latitude regions, may contain population groups highly exposed to some of these pollutants. Significant differences in the concentrations of these compounds have been found between the two cohorts. Differences in maternal population such as age or body mass index cannot explain this variation. One possible cause of variability is the seven year time period elapsed between the two cohort recruitments but the strong differences observed do not allow exclusion of local diet differences. Thus, the different average PCB congener distributions between the two cohorts suggests an influence from materials containing diverse PCB mixtures. The congener mixtures found in Menorca could reflect a diet contribution from some western Mediterranean fish species. These results provide baseline information on prenatal OHC background levels in the Mediterranean area.

1. Introduction

Organohalogen Compounds (OHCs) such as DDTs, hexachlorocyclohexanes (HCHs), hexachlorobenzene (HCB), polychlorobiphenyls (PCBs) and polybromodiphenyl ethers (PBDEs) are widespread toxic environmental pollutants which have been extensively used as pesticides, flame retardants, hydraulic fluids and in many other industrial applications[1]. OHCs have been released into the environment as a consequence of human activity for many years. They are persistent, ubiquitous and highly lipophilic so they bioacumulate and biomagnify through the food chain[2].

In Spain and in many other western countries, use of organochlorine compounds (OCs) started in the 1930s and lasted until the end of the 1970s when they were highly restricted. In contrast, PBDE production was initiated in 1970s. Manufacture of the technical penta- and octa-BDE mixtures ceased around 2004[3] but production of decaBDE is still going. Some commercial mixtures of these compounds are still in use[4]. In 2004, the Stockholm Convention (SC) on Persistent Organic Pollutants (POPs) banned twelve of these compounds[5], including PCBs, DDT and HCB. However, use of DDT for malaria control is still in use in tropical areas. In the last few years, some new pollutants have been added to the above mentioned list, such as certain components of the pentaBDE and octaBDE mixtures and α-, β- and γ-HCH isomers[6]. As a consequence of these regulatory restrictions, OC levels have diminished in biota and human tissues in many countries[7]. Concerning PBDEs, the observed trends do not show a common feature[8,9].

OHC monitoring in humans during the early age stages is important. During pregnancy these compounds are transferred from mother to fetus through the placenta[10]. Fetuses are more vulnerable than adults as their immune systems and detoxification mechanisms are not fully developed. OHCs may therefore cause damage and may predispose to prospective health problems[11]. Previous studies have shown that exposure to certain OHCs may influence fetal and early childhood growth[12] or fetal loss[13]. It has also been shown that some of these compounds have deleterious effects on attention in the school period[14] and on social behaviour at 4 years of age[15].

In Mediterranean countries there is very limited information on prenatal exposure to OHCs[16-19]. Furthermore, the available information needs to be discussed in terms of geographic variability and possible temporal differences related to the periods of use of these compounds, namely OCs vs PBDEs.

In order to contribute to fill this gap, concentrations of OHCs in cord blood serum from two Mediterranean Spanish cohorts, Valencia and Menorca (Fig. 1), are described in the present study. Cord blood serum taken upon child birth is a good medium for description of the in utero exposure to the OCH. They provide information of the exposure levels in this first life stage.

The island of Menorca is a popular tourist destination with strong agricultural activities. Cattle rising for milk production is important, which has involved an extensive use of the land for pasture[20]. The island does not contain any large factory. A portion of the inhabitants are fishermen and people have easy access to fish and seafood. The hospital where mothers and children were recruited belongs to the public health service of the Balearic Islands and collects a large proportion of the births in the whole island.

Valencia is a coastal city located in the eastern shore of the Iberian Peninsula. The cohort was recruited in Hospital La Fe which belongs to the public health system of the Valencian Community. This hospital gives service to an area of 1372 km^2 (Fig. 1) including 34 municipalities with a reference population of approximately 300,000 inhabitants. This population has wide socio-demographic and environmental heterogeneity that can be divided into an urban zone (city of Valencia), a densely populated metropolitan zone, a semi-urban zone encompassing industrial and agricultural activities as well as residential areas, and a wide rural zone in which extensive aquiculture is developed. No large factories are located in the area. Fish is also a common constituent in the diet of people belonging to these four groups.

The distance between the two cohort locations is about 400 km. Both communities are situated in typical Mediterranean sites and can be assumed to have similar exposure scenarios. The mothers living in these areas are likely exposed to baseline OHC levels of western Mediterranean locations.

The present study is devoted to describe the OHC concentrations in cord blood serum of these communities and to identify their similarities and differences providing a reference standard for other populations from Mediterranean areas and from other biogeographical groups.

2. Material and Methods

2.1 Populations and recruitment

The participant newborns in our population of study (n = 265) were recruited in the context of the cross-sectional INMA project (Spanish Children´s Health and Environment) which is a prospective multi-center pregnancy and birth cohort study on general population[21]. The present work includes the analysis of two INMA cohorts, Valencia and Menorca (Fig. 1). The Menorca cohort recruited all women presenting for antenatal care over 12 months from mid 1997 to 1998. 482 children were enrolled. The study design details are reported elsewhere[22]. Here data for a subset of 91 newborns is presented. In the Valencia cohort, deliveries took place between May 2004 and February 2006. During this period 787 women gave birth to a live infant. 500 of them allowed collection of cord blood for OHCs analysis[23]. Here we report OHC levels for a subset of 174 newborns. All mothers who agreed to participate in either study signed a written informed consent before inclusion. Both Valencia and Menorca protocols were approved by their respective ethics committees, the former in Hospital La Fe and the latter in the Municipal Institute of Medical Research from Barcelona.

2.2 Materials

Materials, laboratory analytical methods and quality control procedures have been described elsewhere[24]. Standards of tetrabromobenzene (TBB), PCB 209, PCB 142 and PCB 200 were purchased from Dr Ehrenstorfer GmbH (Wesel, Germany). α-HCH, β-HCH, γ-HCH, δ-HCH, HCB, pentachlorobenze (PeCB), 4,4'-DDT, 2,4’-DDT and their metabolites, 4,4’-DDE, 2,4’-DDE, 4,4’-DDD, 2,4’-DDD, and PCBs (congeners 28, 52, 101, 118, 153, 138 and 180) were also purchased from Dr Ehrenstorfer. The PBDE standards were contained in two analytical solutions, EO-5099 (BDE 1, 2, 3, 7, 8, 10, 11, 12, 13, 15, 17, 25, 28, 30, 32, 33, 35, 37, 47, 49, 66, 71, 75, 77, 85, 99, 100, 116, 118, 119, 126, 138, 153, 154, 155, 166, 181, 183 and 190) and EO-5103 (BDE 17, 28, 47, 66, 71, 85, 99, 100, 153, 154, 138, 183, 190 and 209), that were purchased from Cambridge Isotope Laboratories, Inc (Andover, MA, USA). ^{13}C-BDE 209 and BDE 118 were purchased in a certified standard (50 µL/mL). All standard solutions were of 98% purity at least. They were prepared in isooctane for trace organic analysis. This isooctane and analytical grade concentrated sulfuric acid and *n*-hexane were purchased from Merck (Darmstadt, Germany).

2.3 Serum extraction and clean up

Briefly, 1 ml of cord serum was spiked with the surrogate standards TBB and PCB 209 (vortex stirring for 30 s at 2,000 rpm). n-Hexane (3 ml) was added followed by 2 ml of concentrated sulfuric acid. After reaction, the mixture was stirred for 30 s and the supernatant n-hexane phase was separated by centrifugation. The remaining sulfuric acid solution was re-extracted two times with 2 ml of n-hexane (stirring 30 s). The combined n-hexane extracts (7 ml) were additionally cleaned with 2 ml of sulfuric acid (stirring 30 s). Then, the n-hexane phase was separated and reduced to dryness under a gentle nitrogen stream. The extract was transferred to gas chromatography (GC) vials using four rinses of 25 µl of isooctane. PCB 142 was added as injection standard for OHCs analysis.

2.4 Lipid determination

In the samples from the Menorca cohort, total serum lipids were determined by gravimetry[17]. In the Valencia cohort sample lipid concentrations were calculated from total cholesterol and triglycerides[25]. These compounds were measured in the General Biochemistry Laboratory of Hospital La Fe using enzymatic methods.

2.5 Analysis of organochlorine compounds

OC concentrations were determined by GC with electron capture detection (GC-ECD) using an Agilent 6890N GC with a Micro-ECD (Agilent Technologies, Palo Alto, CA, USA) equipped with a DB-5 fused silica capillary column of 60 m length, 0.25 mm internal diameter and 0.25 µm film thickness (J & W Scientific, Folsom, Ca, USA). Details on operating conditions, identification, quantification and quality control procedures have already been described[24].

2.6 Analysis of polybromodiphenyl ethers

After OC analysis by GC-ECD, vials samples were re-evaporated under a nitrogen stream and 20 µl of BDE 118 and 10µl of [^{13}C]-BDE 209 were added as internal standards. PBDEs from the Valencian cohort were determined using an Agilent 6890N GC coupled to a 5975 mass spectrometer (GC-MS) (Agilent Technologies) operating in electron capture negative ionization (ECNI) mode. The instrument was equipped with a low bleed SGE-BPX5 MS fused silica capillary column (15 m length, 0.25 mm internal diameter and 0.10 µm film thickness). PBDEs from the Menorca cohort were determined with a HP 5973 MSD GC-MS (Agilent Technologies) operating in NICI mode. Samples were injected in splitless mode onto a DB-5 fused silica capillary column of 60 m length, 0.25 mm internal diameter and 0.25 µm film thickness (J & W Scientific). Details on operating conditions, identification and quantification processes have been described elsewhere[24,26].

2.7 Reference materials

Reference materials obtained from the Arctic Monitoring and Assessment Program (AMAP) were used to assess precision and accuracy of the analytical methods used. The laboratory is in compliance with the AMAP Ring Test Proficiency Program for persistent organic pollutants in human serum including lipid analysis (Institut National de Santé Publique du Québec, Canada).

2.8 Data analysis

Standard descriptive statistics were calculated for OHC concentrations. OHCs values were lipid-adjusted dividing serum residue levels by total serum lipid. A value of zero was used for data analysis when measurable quantities of the analytes were below limit of detection. For comparison, descriptive analysis was limited to contaminants which were measured in the two cohorts. The Mann-Whitney U test was used to examine OHC differences between the two cohorts. Statistical significance was considered at $p<0.05$ (two sided). Statistical analysis was performed with the Statistical Package for Social Sciences version 15.0 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Population of study

The characteristics of the maternal and newborn participants in the cohorts of Valencia and Menorca are described in Table 1. When using standardized categories for body mass index (BMI), a significant higher proportion of overweight (>26 kg/m^2) and obese mothers (>30 kg/m^2) were found in the Valencian cohort (29.9% and 10.9% respectively) than in Menorca (12.1% and 3.3%, respectively). Thus, the average BMI was statistically significantly higher in Valencia than in Menorca (Table 1). Mothers from Menorca (average age 28.5 yr) were slightly younger than those from Valencia (average age 30.1 yr) and the difference was statistically significant (Table 1). The main difference concerned the proportion of mothers older than 35 yr which was higher in Valencia (18.4%) than in Menorca (4.4%). No statistically significant differences were observed in other maternal features such as previous lactation and education level.

The newborn characteristics of both cohorts were comparable concerning gender, gestational age and birth weight. However, the Valencian newborns were significantly taller than those from Menorca (Table 1).

3.2 Concentrations of polybromodiphenyl ethers

Means, standard deviations, medians, percentiles and concentration ranges of the PBDE congeners analyzed and found in concentrations above quantification limits in the Valencia and Menorca cohorts are shown in Table 2. The distributions are dominated by BDE 47 contributing to 38% and 51% of total PBDE in Valencia and Menorca, respectively (Fig. 2). BDE 99 and BDE 100 are the second most abundant congeners (Table 2). In contrast, BDE 153 is not found in any of the Menorca cohort samples while it is observed in 52% of the samples from the cohort of Valencia (Fig. 2). BDE 183 is found in both cohorts but in much higher proportion in Valencia (~5%) than in Menorca (~1%). In both cases, the observed distributions essentially correspond to the commercial pentaPBDE mixtures. The higher proportion of BDE

183 in the cohort of Valencia suggest some small contributions of octaPBDE in this area.

The mean values of total PBDEs are 11 and 5.4 ng/g lipids in Valencia and Menorca, respectively (Table 2). The median values provide more representative figures for comparison with previously reported data from other cohorts. These values, 2.8 and 6.8 ng/g lipid in Menorca and Valencia cohorts, respectively, are low in comparison to other studies (Table 3). Thus, median concentrations in the range of 18.4-39 ng/g lipid have been reported in cord blood serum from several cohorts from the USA[32-35]. Median concentrations above 10 ng/g lipid have also been reported in Madrid (Spain)[18], Toulouse (France)[27] and Guiyu (China)[38] (Table 3). Intermediate median concentrations between the Valencian and Menorcan values, 3.3-3.9 ng/g lipid, have been reported in Singapore[36], South China[28] and Groningen (The Netherlands)[30]. Median PBDE concentrations below those observed in the cohort of Menorca have only been reported in Sweden, Copenhagen (Denmark) and Japan, 1.69, 0.95 and 0.65 ng/g lipid, respectively[29,31,37] (Table 3).

3.2 Concentrations of polychlorobiphenyls

Means, standard deviations, medians, percentiles and concentration ranges of the PCB congeners analyzed in the cohorts of Valencia and Menorca are shown in Table 4. The distributions are dominated by CB 180 in Menorca and CB 153 and CB138 in Valencia (Fig. 3). The higher chlorinated congeners, CB 118, CB 153, CB 138 and CB 180, are those most abundant in both cohorts (Fig. 3). The median concentrations of total PCBs (the seven congener analyzed) in Valencia, 0.38 ng/ml (150 ng/g lipid), are nearly half those in Menorca, 0.65 ng/ml (240 ng/g lipid). The concentrations from the cohort of Menorca are higher than those reported in many other sites (Table 5)[10,31,32,39,41-57] except Michalovce (Slovakia)[45] and Chukotka (Russia)[48]. The cohort from Valencia exhibits concentrations more in the average. Besides the above mentioned populations, they are lower than those described in North Netherlands[44], Faroe Islands[47], Quebec[50] and Northern Quebec[49], and Zhejiang (China)[55].

3.3. Concentrations of hexachlorobenzene

Statistical data of the concentrations of HCB in both cohorts are shown in Table 6. The median values of Valencia, 0.24 ng/ml (47 ng/g lipid), are less than half those in Menorca, 0.68 ng/ml (260 ng/g lipid). Pentachlorobenzene was found above limit of detection in less than 10% of the samples from both cohorts. These data are therefore not reported. The observed HCB concentrations in the cohort of Menorca are high in comparison with those found in previous studies (Table 5). Only the cord blood concentrations from Ribera d'Ebre (Catalonia, Spain)[10] exhibit higher values than Menorca. However, Ribera d'Ebre cohort belongs to a geographical area that contains the village of Flix whose inhabitants exhibit the highest HCB concentrations ever described in general population[58-60] as a consequence of the emissions from a chloro-alkali factory. The high concentrations found in newborns of Ribera d'Ebre[10] is consistent with these previous observations. Considering previous studies (Table 5), the concentrations in the cohort of Valencia are also high. Besides Ribera d'Ebre[10], the only literature references describing higher cord blood concentrations than in Valencia refer to Chukotka (Russia)[48] or Veracruz (Mexico)[52]. The high values from the Valencian and Menorcan cohorts are consistent with the HCB levels of Spanish general population (not newborns) described in previous studies that are higher than in other European countries[61].

3.4. Concentrations of hexachlorocychlohexanes

Statistical data on the concentrations of β-HCH in the cohorts of Valencia and Menorca are shown in Table 6. γ-HCH, δ-HCH and α-HCH were found above detection limit in less than 10% of the samples and therefore are not included in the Table. The median concentrations in the cohort from Menorca, 0.19 ng/ml (60 ng/g lipid), are again higher than those from Valencia, 0.092 ng/ml (35 ng/g lipid). These concentrations are lower than those found in cohorts from sites such as Ribera d'Ebre (Catalonia, Spain)[10], Chukotka (Russia)[48], Veracruz (Mexico)[52], Rio de Janeiro (Brazil)[53], New Delhi (India)[56] or Singapore[57] and higher than those found in Wielkopolska (Poland)[46], Artic Canada[51], Chiba and Yamanashi (Japan)[54] or Zhejiang (China)[55].

3.5. Concentrations of DDTs

The concentrations of 4,4'-DDE and 4,4'-DDT are also reported in Table 6. The median values in Valencia were 0.53 ng/ml (210 ng/g lipid) and below limit of detection for 4,4'-DDE and 4,4'-DDT, respectively. In Menorca they were 0.94 ng/ml (360 ng/g lipid) and 0.03 ng/ml (11 ng/g lipid) for 4,4'-DDE and 4,4'-DDT, respectively. The higher concentrations of 4,4'-DDE than 4,4'-DDT are consistent with an old origin of this mixture of pollutants since the latter is the one used as pesticide and the former is a transformation compound. The observed concentrations of 4,4'-DDE in these two cohorts are lower than those found in countries that have recently used DDT for Malarian control such as Oaxaca (Mexico)[41], Veracruz (Mexico)[52] and New Delhi (India)[56] but higher than those found in other sites such as Brescia (Italy)[39], Flanders (Belgium)[42], Faroe Islands (Denmark)[47], Quebec (Canada)[50], Arctic Canada[51], Maryland (USA)[32], Rio de Janeiro (Brazil)[53], Chiba and Yamanashi (Japan)[54] or Zhejiang (China)[55]. Intermediate values between those in Valencia and Menorca have been reported in Ribera d'Ebre (Catalonia, Spain)[10], Wielkopolska (Poland)[46], Chukotka (Russia)[48], Northern Quebec (Canada)[49] and Singapore[57].

4. Discussion

In Spain OC pesticides were widely used from 1950 until mid seventies, although specific informations on the zones considered in this study are very scarce. The two areas are characterized for having a strong agricultural activity and most likely OC pesticides were intensively used. The observed DDT/DDE ratios are very low, 0.08 in both cohorts, indicating old exposure.

The distributions of HCB, β-HCH, total DDTs, total PCBs and total PBDEs (Figure 4) are statistically different between the two cohorts according to the Mann-Whitney U test. As mentioned in the results section, the median concentration differences between the cohorts of Valencia and Menorca are significant. Comparison of the maternal characteristics between the two cohorts showed significant differences for age and BMI but not for the records of previous lactation or educational level.

Mothers from Menorca were statistically significantly younger than those from Valencia, 28.5 and 30.1 yr, respectively. Statistically significant associations between higher concentrations of OCs in cord blood and older maternal age have been found for HCB[50,62,63], 4,4’-DDE[10,50,62], 4,4’-DDT[62], β-HCH[62] and PCBs[32,50,62,63]. This trend is the opposite between maternal age and cord blood concentration differences of the cohorts of Valencia and Menorca. Average maternal ages of the two cohorts cannot therefore justify the observed cord blood differences.

On the other hand, while several previous studies did not find any association between maternal age and cord blood PBDE concentrations, a negative trend was found with statistical significance in one of them, involving lower PBDE concentrations in cord blood at higher maternal age[32]. According to these results, maternal age differences here are not explaining differences on PBDE levels in the cohorts of Valencia and Menorca since mothers from Menorca are younger.

The mothers from the cohorts of Menorca exhibit statistically significantly lower BMI than those from the cohort of Valencia, 22.5 and 24.3 kg/m^2, respectively. Previous studies have shown higher cord blood concentrations of HCB[62], 4,4’-DDE[62], 4,4’-DDT[62] and PBDEs[32] and lower concentrations of PCBs[32] at higher maternal BMI. These previous results are in agreement with the cord blood concentrations differences between Valencia and Menorca for PBDEs and PCBs but not for HCB and DDTs.

Other maternal indicators such as previous lactation or education level do not show significant differences between the two cohorts. They are therefore unlikely causes of variation.

One distinct feature of the cord blood OHC concentration differences of these two cohorts is the strong grouping of organochlorine and organobromine compounds, which exhibit higher OC levels in Menorca than Valencia (Tables 4 and 6), and show higher PBDEs levels in Valencia than Menorca (Table 2). This contrast is observed irrespectively of OC origin, either agricultural or industrial. This OHC grouping may reflect temporal differences in the recruitment of the newborns from the two cohorts. The use of the above mentioned OCs has declined as consequence of legal regulations[5] which were aimed to decrease DDTs, PCBs, HCHs and HCB. In contrast, PBDE use increased after OC restriction and actions to decrease their environmental impact have only been implemented recently. This time delay in banning organochlorine and organobromine groups is consistent with the earlier collection of cord blood samples in Menorca than in Valencia.

Studies of temporal trends of OHC in the area are very scarce. One recent paper reported a general decrease in PCB concentrations in breast milk samples collected between 1998 and 2007 in Catalonia[64], a region located north of Valencia. These results are consistent with those observed in other studies concerning countries submitted to the same OC regulations as Spain showing a common decreasing trend of OC concentrations in human tissues[65-67]. However, the OC medians of the two cohorts involve concentration differences of about two times, e.g. 0.38 and 0.65 ng/ml for PCBs, 0.24 and 0.68 ng/ml for HCB, 0.092 and 0.19 ng/ml for β-HCH or 0.53 and 0.94 ng/ml for 4,4'-DDE in Valencia and Menorca, respectively. These strong differences are difficult to attribute to the single effect of cord blood collection from babies born in a seven year interval. Possibly, additional effects such as local differences or others may also determine the OHC concentrations of newborns from the two cohorts.

In this respect, the average congener PCB distributions of Valencia and Menorca are clearly different (Fig. 3). While CB 153 and CB 138 are found in higher proportion than CB 180 in the former, CB 180 is the predominant congener in the latter. This contrast suggests an influence from different PCB sources in both cohorts. As indicated above, fish and sea food are common elements of the diet in both of them. However, in Menorca fish is essentially obtained from local fishing activities developed in the western Mediterranean whereas in Valencia consumption is essentially related to the general Spanish market trading which includes a significant proportion of fish from the Atlantic Ocean. The PCB distributions of some fish from the western Mediterranean exhibit a high proportion of CB 180[68].

Abbreviations

Stockholm Convention (SC), Persistent Organic Pollutants (POPs), Organohalogen compounds (OHCs), organochlorine compounds (OCs), organochlorine pesticides (OCPs), hexachlorocyclohexanes (HCHs), hexachlorobenzene (HCB), pentaclorobenzene (PeCB), polychlorobiphenyls (PCBs), polybromodiphenyl ethers (PBDEs), tetrabromobenzene (TBB), gas chromatography (GC), GC with electron capture detection (GC-ECD), gas chromatograph coupled to a mass spectrometer (GC-MS), electron capture negative ionization (ECNI), Spanish Children´s Health and Environment (INMA).

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References

1. M. Alaee, P. Arias, A. Sjodin and I. Bergman, An overview of commercially used brominated flame retardants, their applications, their use patterns in different countries/regions and possible modes of release, *Environ. Int.*, 2003, **29**, 683-689.
2. A. Sjödin, L. Hagmar, E. Klasson-Wehler, J. Björk and I. Bergman, Influence of the consumption of fatty Baltic Sea fish on plasma levels of halogenated environmental contaminants in Latvian and Swedish men, *Environ. Health Perspec.*, 2000, **108**, 1035-1041.
3. http://www.bsef.com/uploads/Documents/documents/BSEF%20Statement%20COP4.pdf (15/10/2009)
4. http://www.ebfrip.org/main-nav/european-regulatory-centre/rohs-directive-restriction-of-the-use-of-certain-hazardous-substances-in-electrical-and-electronic-equipment/the-rohs-directive-and-deca-bde/ (15/10/2009),
5. http://chm.pops.int/ (last accessed June 22, 2010).
6. http://chm.pops.int/Convention/tabid/54/language/en-US/Default.aspx#convtext (last accessed June 22, 2010).
7. A. Bignert, M. Olsson, W. Persson, S. Jensen, S. Zakrisson, K. Litzen, U. Eriksson, L. Häggberg and T. Alsberg, Temporal trends of organochlorines in Northern Europe, 1967-1995. Relation to global fractionation, leakage from sediments and international measures, *Environ. Pollut.,* 1998, **99**, 177-198.

8. R. J. Law, D. Herzke, S. Harrad, S. Morris, P. Bersuder and C. R. Allchin, Levels and trends of HBCD and BDEs in the European and Asian environments, with some information for other BFRs, *Chemosphere*, 2008, **73**, 223-241.
9. S. Lignell, M. Aune, P. O. Darnerud, S. Cnattingius and A. Glynn, Persistent organochlorine and organobromine compounds in mother's milk from Sweden 1996-2006: Compound-specific temporal trends, *Environ. Res.,* 2009, **109**, 760-767.
10. M. Sala, N. Ribas-Fitó, E. Cardo, M. E. De Muga, E.; Marco, C. Mazón, A. Verdú, J. O. Grimalt and J. Sunyer, Levels of hexachlorobenzene and other organochlorine compounds in cord blood: Exposure across placenta, *Chemosphere*, 2001, **43**, 895-901.
11. B. C. Gladen, W. J. Rogan, P. Hardy, J. Thullen, J. Tingelstad and M. Tully, Development after exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene transplacentally and through human milk, *J. Pediatr.,* 1988, 113, 991-995.
12. I. Hertz-Picciotto, M. J. Charles, R. A. James, J. A. Keller, E. Willman and S. Teplin, In utero polychlorinated biphenyl exposures in relation to fetal and early childhood growth, *Epidemiology*, 2005, **16**, 648-656.
13. M. P. Longnecker, M. A. Klebanoff, D. B. Dunson, X. Guo, Z. Chen, H. Zhou and J. W. Brock, Maternal serum level of the DDT metabolite DDE in relation to fetal loss in previous pregnancies, *Environ. Res.,* 2005, **97**, 127-133.
14. J. L. Jacobson and S. W. Jacobson, Prenatal exposure to polychlorinated biphenyls and attention at school age, *J. Pediatr.,* 2003, **143**, 780-788.
15. N. Ribas-Fitó, M. Torrent, D. Carrizo, J. Júlvez, J. O. Grimalt and J. Sunyer, Exposure to hexachlorobenzene during pregnancy and children's social behavior at 4 years of age, *Environ. Health Perspec.*, 2007, **115**, 447-450.
16. D. Carrizo, J. O. Grimalt, N. Ribas-Fito, J. Sunyer and M. Torrent, Physical-chemical and maternal determinants of the accumulation of organochlorine compounds in four-year-old children, *Environ. Sci. Technol.,* 2006, **40**, 1420-1426.
17. D. Carrizo, J. O. Grimalt, N. Ribas-Fito, J. Sunyer and M. Torrent, Influence of breastfeeding in the accumulation of polybromodiphenyl ethers during the first years of child growth, *Environ. Sci. Technol.,* 2007, **41**, 4907-4912.

18. B. Gómara, L. Herrero, J. J. Ramos, J. R. Mateo, M. A. Fernández, J. F. Garcia and M. J. Gonzalez, Distribution of polybrominated diphenyl ethers in human umbilical cord serum, paternal serum, maternal serum, placentas, and breast milk from madrid population, Spain, *Environ. Sci. Technol.,* 2007, **41**, 6961-6968.
19. M. J. Lopez-Espinosa, A. Granada, J. Carreno, M. Salvatierra, F. Olea-Serrano and N. Olea, Organochlorine Pesticides in Placentas from Southern Spain and Some Related Factors, *Placenta*, 2007, **28**, 631-638.
20. D. Carrizo, J. O. Grimalt, N. Ribas-Fito, M. Torrent and J. Sunyer, In utero and post-natal accumulation of organochlorine compounds in children under different environmental conditions, *J. Environ. Monitor.,* 2007, **9**, 523-529.
21. N. Ribas-Fito, R. Ramón, F. Ballester, J. O. Grimalt, A. Marco, N. Olea, M. Posada, M. Rebagliato, A. Tardón, M. Torrent and J. Sunyer, Child health and the environment: The INMA Spanish study, *Paediatr. Perinat. Ep.*, 2006, **20**, 403-410.
22. S. Polk, J. Sunyer, L. Muñoz-Ortiz, M. Barnes, M. Torrent, C. Figueroa, J. Harris, O. Vall, J. M. Antón and P. Cullinan, A prospective study of Fel d1 and Der p1 exposure in infancy and childhood wheezing, *Am. J. Resp. Crit. Care,* 2004, **170**, 273-278.
23. M. J. Lopez-Espinosa, E. Vizcaino, M. Murcia, V. Fuentes, A. M. Garcia, M. Rebagliato, J. O. Grimalt and F. Ballester, Prenatal exposure to organochlorine compounds and neonatal thyroid stimulating hormone levels, *J. Expo. Sci. Environ. Epidemiol.,* 2010, **20,** 579–588.
24. J. O. Grimalt, M. Howsam, D. Carrizo, R. Otero, M. R. De Marchi and E. Vizcaino, Integrated analysis of halogenated organic pollutants in sub-millilitre volumes of venous and umbilical cord blood sera, *Anal. Bioanal. Chem.,* 2010, **396**, 2265-2272.
25. D. L. Phillips, J. L. Pirkle, V. W. Burse, J. T. Bernert Jr, L. O. Henderson and L. L. Needham, Chlorinated hydrocarbon levels in human serum: Effects of fasting and feeding, *Arch. Environ. Con. Tox.,*1989, **18**, 495-500.
26. E. Vizcaino, L. Arellano, P. Fernandez and J. O. Grimalt, Analysis of whole congener mixtures of polybromodiphenyl ethers by gas chromatography-mass spectrometry in both environmental and biological samples at femtogram levels, *J. Chromatogr. A,* 2009, **1216,** 5045-5051.

27. J. P. Antignac, R. Cariou, D. Zalko, A. Berrebi, J. P. Cravedi, D. Maume, P. Marchand, F. Monteau, A. Riu, F. Andre and B. Le Bizec, Exposure assessment of French women and their newborn to brominated flame retardants: Determination of tri- to deca- polybromodiphenylethers (PBDE) in maternal adipose tissue, serum, breast milk and cord serum, *Environ. Pollut.,* 2009, **157**, 164-173.

28. X. Bi, W. Qu, G. Sheng, W. Zhang, B. Mai, D. Chen, L. Yu, J. Fu, Polybrominated diphenyl ethers in South China maternal and fetal blood and breast milk, *Environ. Pollut.,* 2006, **144**, 1024-1030.

29. Y. Kawashiro, H. Fukata, M. Omori-Inoue, K. Kubonoya, T. Jotaki, H. Takigami, S. I. Sakai, C. Mori, Perinatal exposure to brominated flame retardants and polychlorinated biphenyls in Japan, *Endocr. J.*, 2008, **55**, 1071-1084.

30. L. Meijer, J. Weiss, M. Van Velzen, A. Beouwer, Ã. K. E. Bergman, P. J. J. and Sauer, Serum concentrations of neutral and phenolic organohalogens in pregnant women and some of their infants in the Netherlands, *Environ. Sci. Technol.,* 2008, **42**, 3428-3433.

31. D. Meironyté Guvenius, A. Aronsson, G. Ekman-Ordeberg, A. Bergman and K. Norën, Human prenatal and postnatal exposure to polybrominated diphenyl ethers, polychlorinated biphenyls, polychlorobiphenylols, and pentachlorophenol, *Environ. Health Perspect.,* 2003, **111**, 1235-1241.

32. J. B. Herbstman, A. Sjödin, B. J. Apelberg, F. R. Witter, D. G. Patterson, R. U. Halden, R. S. Jones, A. Park, Y. Zhang, J. Heidler, L. L. Needham and L. R. Goldman, Determinants of prenatal exposure to polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in an urban population, *Environ. Health Perspect.,* 2007, **115**, 1794-1800.

33. A. Mazdai, N. G. Dodder, M. P. Abernathy, R. A. Hites and R. M. Bigsby, Polybrominated diphenyl ethers in maternal and fetal blood samples, *Environ. Health Perspect.,* 2003, **111**, 1249-1252.

34. X. Qiu, R. M. Bigsby and R. A. Hites, Polybrominated diphenyl ethers in human blood samples from the United States, *Environ. Health Perspect.,* 2009, **117**, 93-98.

35. J.B. Herbstman, A. Sjödin, M. Kurzon, S.A. Lederman, R.S. Jones, V. Rauh, L.L. Needham, D. Tang, M, Niedzwiecki, R.Y. Wang and F. Perera, Prenatal

exposure to PBDEs and neurodevelopment, *Environ Health Perspect*., 2010, **118**, 712-719.

36. J. Tan, A. Loganath, Y.S. Chong and J.P. Obbard, Exposure to persistent organic pollutants in utero and related maternal characteristics on birth outcomes: A multivariate data analysis approach. *Chemosphere*, 2008, **74**, 428-433.

37. M. Frederiksen, C. Thomsen, M. Frøshaug, K. Vorkamp, M. Thomsen, G. Becher and L.E. Knudsen, Polybrominated diphenyl ethers in paired samples of maternal and umbilical cord blood plasma and associations with house dust in a Danish cohort. *Int J Environ Health,* 2010, **213,** 233-242.

38. K. Wu, S. Xu, J. Liu, Y. Guo, Y. Li and X. Huo, Polybrominated diphenyl ethers in umbilical cord blood and relevant factors in neonats from Guiyu, China, *Environ. Sci. Technol.,* 2010, **44,** 813-819.

39. R. Bergonzi, C. Specchia, M. Dinolfo, C. Tomasi, G. De Palma, T. Frusca and P. Apostoli, Distribution of persistent organochlorine pollutants in maternal and foetal tissues: Data from an Italian polluted urban area, *Chemosphere*, 2009, **76**, 747-754.

40. A. Covaci, P. Jorens, Y. Jacquemyn and P. Schepens, Distribution of PCBs and organochlorine pesticides in umbilical cord and maternal serum, *Sci. Total Environ.,* 2002, **298**, 45-53.

41. A. Barraza-Vázquez, V. H. Borja-Aburto, S. Bassol-Mayagoitia, A. Monrroy and R. Recio-Vega, Dichlorodiphenyldichloroethylene concentrations in umbilical cord of newborns and determinant maternal factors, *J. Appl. Tox.,* 2008, **28**, 27-34.

42. G. Koppen, E. Den Hond, V. Nelen, E. Van De Mieroop, L. Bruckers, M. Bilau, H. Keune, N. Van Larebeke, A. Covaci, H. Van De Weghe, C. Schroijen, K. Desager, M. Stalpaert, W. Baeyens and G. Schoeters, Organochlorine and heavy metals in newborns: Results from the Flemish Environment and Health Survey (FLEHS 2002-2006), *Environ. Int.*, 2009, **35**, 1015-1022.

43. C. Koopman-Esseboom, M. Huisman, N. Weisglas-Kuperus, C. G. Van Der Paauw, L. G. M. T. Tuinstra, E. R. Boersma and P. J. J. Sauer. PCB and dioxin levels in plasma and human milk of 418 dutch women and their infants.

Predictive value of PCB congener levels in maternal plasma for fetal and infant's exposure to PCBs and dioxins. *Chemosphere*, 1994, **28,** 1721-1732.

44. S. D. Soechitram, M. Athanasiadou, L. Hovander, Ã. Bergman and P. J. J. Sauer. Fetal Exposure to PCBs and their Hydroxylated Metabolites in a dutch Cohort. *Environ. Health Perspect.*, 2004, **112,** 1208-1212.

45. J. S. Park, A. Bergman, L. Linderholm, M. Athanasiadou, A. Kocan, J. Petrik, B. Drobna, T. Trnovec, M. J. Charles and I. Hertz-Picciotto. Placental transfer of polychlorinated biphenyls, their hydroxylated metabolites and pentachlorophenol in pregnant women from eastern Slovakia. *Chemosphere*, 2008, **70,** 1676-1684.

46. K. Jaraczewska, J. Lulek, A. Covaci, S. Voorspoels, A. Kaluba-Skotarczak, K. Drews and P. Schepens. Distribution of polychlorinated biphenyls, organochlorine pesticides and polybrominated diphenyl ethers in human umbilical cord serum, maternal serum and milk from Wielkopolska region, Poland. *Sci. Total Environ.*, 2006, **372,** 20-31.

47. D. B. Barr, P. Weihe, M. D. Davis, L. L. Needham and P. Grandjean. Serum polychlorinated biphenyl and organochlorine insecticide concentrations in a Faroase birth cohort. *Chemosphere*, 2006, **62,** 1167-1182.

48. E. Eik Anda, E. Nieboer, A. A. Dudarev, T. M. Sandanger and J. Ø. Odland. Intra-and intercompartmental associations between levels of organochlorines in maternal plasma, cord plasma and breast milk, and lead and cadmium in whole blood, for indigenous peoples of Chukotka. *J. Environ. Monit.*, 2007, **9,** 884-893.

49. G. Muckle, P. Ayotte, E. Dewailly, S. W. Jacobson and J. L. Jacobson. Prenatal exposure of the northern Québec Inuit Infants to Environmental Contaminants. *Environ. Health Perspect.*, 2001, **109,** 1291-1299.

50. M. Rhainds, P. Levallois, E. Dewailly and P. Ayotte. Lead, mercury and organochlorine compound levels in cord blood in Québec, Canada. *Arch. Environ. Health*, 1999, **54,** 40-47.

51. J. Butler Walker, L. Seddon, E. McMullen, J. Houseman, K. Tofflemire, A. Corriveau, J. P. Weber, C. Mills, S. Smith and J. Van Oostdam. Organochlorine levels in maternal and umbilical cord blood plasma in Arctic Canada. *Sci. Total Environ.*, 2003, **302,** 27-52.

52. S. M. Waliszewski, A. A. Aguirre, R. M. Infanzon, C. S. Silva and J. Siliceo. Organochlorine Pesticide Levels in Maternal Adipose Tissue, Maternal Blood Serum, Umbilical Blood Serum, and Milk from Inhabitants of Veracruz, Mexico. *Arch. Environ. Contam. Toxicol.*, 2001, **40,** 432-438.

53. P. N. Sarcinelli, A. C. S. Pereira, S. A. Mesquita, J. J. Oliveira-Silva, A. Meyer, M. A. C. Menezes, S. R. Alves, R. C. O. C. Mattos, J. C. Moreira and M. Wolff. Dietary and reproductive determinants of plasma organochlorine levels in pregnant women in Rio de Janeiro. *Environ. Res.* 2003, **91,** 143-150.

54. H. Fukata, M. Omori, H. Osada, E. Todaka and C. Mori. Necessity to Measure PCBs and Organochlorine Pesticide Concentrations in Human Umbilical Cords for Fetal Esposure Assessment. *Environ. Health Perspect.*, 2005, **113,** 297-303.

55. G. Zhao, Y. Xu, W. Li, G. Han and B. Ling. Prenatal exposures to persistent organic pollutants as measured in cord blood and meconium from three localities of Zhejiang, China, *Sci. Total Environ.*, 2007, **377,** 179-191.

56. R. Pathak, R. S. Ahmed, A. K. Tripathi, K. Guleria, C. S. Sharma, S. D. Makhijani and B. D. Banerjee. Maternal and cord blood levels of organochlorine pesticides: Association with preterm labor. *Clin. Biochem.*, 2009, **42,** 746-749.

57. J. Tan, A. Loganath, Y. S. Chong and J. P. Obbard. Exposure to persistent organic pollutants in utero and related maternal characteristics on birth outcomes: A multivariate data analysis approach. *Chemosphere*, 2009, **74,** 428-433.

58. J.O. Grimalt, J. Sunyer, V. Moreno, O.C. Amaral, M. Sala, A. Rosell, J.M. Antó and J. Albaigés. Risk excess of soft-tissue sarcoma and thyroid cancer in a community exposed to airborne organochlorinated compound mixtures with a high hexachlorobenzene content. *Int. J. Cancer* 1991, **56**, 200-203.

59. M. Sala, J. Sunyer, R. Otero, M. Santiago-Silva, C. Camps and J.O. Grimalt. Organochlorine in the serum of inhabitants living near an electrochemical factory. *Occup. Environ. Med.* 1999, **56**, 152-158

60. M. Sala, J. Sunyer, R. Otero, M. Santiago-Silva, D. Ozalla, C. Herrero, J. To-Figueras, M. Kogevinas, J.M. Antó, C. Camps and J.O. Grimalt. Health effects of chronic high exposure to hexachlorobenzene in a general population sample. *Arch. Environ. Health* 1999, **54**, 102-109

61. R. de Salamanca, A. Lopez-Minas, J. Muñoz, J. To-Figueras and C. Conde. Is hexachlorobenzene human overload related to porphyria cutanea tarda? *Medical Hypotheses* 1990, **33,** 69-71.

62. D. Carrizo, J. O. Grimalt, N. Ribas-Fito, J. Sunyer and M. Torrent. Physical-chemical and maternal determinants of the accumulation of organochlorine compounds in four-year-old children. *Environ. Sci. Technol.* 2006, **40,** 1420-1426.

63. G. M. Lackmann, J. Angerer, U. Salzberger and U. Tollner. Influence of maternal age and duration of pregnancy on serum concentrations of polychlorinated biphenyls and hexachlorobenzene in full-term neonates. *Biol. Neonate* 1999, **76,** 214-219.

64 M. Schuhmacher, H. Kiviranta, P. Ruokojärvi, M. Nadal and J. L. Domingo, Concentrations of PCDD/Fs, PCBs and PBDEs in breast milk of women from Catalonia, Spain: A follow-up study, *Environ. Int.,* 2009, **35**, 607-613.

65 F. Dallaire, E. Dewailly, C. Laliberta, G. Muckle and P. Ayotte, Temporal trends of organochlorine concentrations in umbilical cord blood of newborns from the lower north shore of the St. Lawrence river (Quèbec, Canada), *Environ. Health Perspect.,*2002, **110**, 835-838.

66 L. Hagmar, E. Wallin, B. Vessby, B. A. Jonsson, A. Bergman and L. Rylander, Intra-individual variations and time trends 1991-2001 in human serum levels of PCB, DDE and hexachlorobenzene, *Chemosphere*, 2006, **64**, 1507-1513.

67 K. Norën and D. Meironyte, Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 20-30 years, *Chemosphere*, 2000, **40**, 1111-1123.

68 M. Sole, C. Porte and J. Albaiges, Hydrocarbons, PCBs and DDT in the NW Mediterranean deep-sea fish *Mora moro*, *Deep-Sea Res*, 2001, **48,** 495-513.

Table 1. Maternal and newborn Characterisitcs of Menorca and Valencia cohorts

Variables	**Valencia**	**Menorca**
	(N=174)	**(N=91)**
	Mothers N (%)†	
Age:	30.1(4.8)[a]	28.5(4.4)[a] **
<25	27(15.5)	21(23.1)
25-29	51(29.3)	36(39.6)
30-34	64(36.8)	27(29.7)
≥35	32(18.4)	4(4.4)
Pre-pregnancy BMI[b]:	24.3(4.6)[a]	22.5(3.4)[a] **
Underweight (BMI<18.5)	5(2.9)	4(4.4)
Normal (18.5≤BMI<25)	108(62.1)	68(74.7)
Overweight (25≤BMI<30)	42(24.1)	11(12.1)
Obese (BMI≥30)	19(10.9)	3(3.3)
Previous Lactacion	14.9(30.0)[a]	18.5(14.2)[a]
≤24 weeks	137(78.7)	63(69.2)
>24 weeks	36(20.7)	25(27.2)
Education Level:		
Up to Primary	61(35.1)	39(40.9)
Secondary	68(39.1)	34(37.4)
University	45 (25.9)	15 (16.5)
	Newborns N (%)†	
Sex:		
Male	78(44.8)	45(49.5)
Female	96(55.2)	43(47.3)
Birth-weight (g):	3317(470)[a]	3225(425)[a]
<2500 g	9(5.2)	5(5.5)
≥2500 g	165(94.8)	83(91.2)
Birth lenght (cm)	50.2(2.1)[a]	49.2(1.6)[a] **
Gestagional age (weeks):	39.7(1.5)[a]	39.4(1.5)[a]
<37 weeks	8(4.6)	4(4.4)
≥37 weeks	166(95.4)	87(95.6)

[a]Arithmetic mean ± Standard deviation; [b]BMI=Body mass index; † Numbers do not always sum total number of participants because of missing values. ** P<0.05 (P value from χ^2 –test or Student's T-test)

Table 2. PBDES concentrations in cord blood serum from Menorca and Valencia

Compounds	Mean(SD) [a]	Median	Percentile 25	Percentile 95	Range	Mean(SD) [a]	Median	Percentile 25	Percentile 95	Range
	Valencia (N=174) ng/g lipid					Menorca (N=91) ng/g lipid				
BDE 47	4.1(6.1)	2.4	nd[1]	18	nd-43	2.8(3.5)	2.1	nd[1]	10.4	nd-17
BDE 99	2.7(4.8)	1.5	nd[1]	10	nd-41	1.3(2.2)	nd[3]	nd[3]	5.4	nd-12
BDE 100	2.3(5.3)	nd[1]	nd[1]	11	nd-46	1.1(3.4)	nd[3]	nd[3]	8.5	nd-26
BDE153	1.3(1.8)	nd[2]	nd[2]	4.6	nd-9.8	nd	nd[1]	nd[1]	nd	nd
BDE183	0.6(2.9)	nd[2]	nd[2]	3.6	nd-27	0.05(0.5)	nd[4]	nd[4]	nd	nd-4.8
ΣPBDEs[b]	11(17)	6.5	1.4	42	nd-140	5.4(6.8)	2.8	nd	18	nd-33

[a] Arithmetic mean (standard deviation); [b] Sum of PBDE congeners analyzed individually; nd: below limit of detection: [1]<0.003 ng/mL; [2]<0.002 ng/mL; [3]<0.006 ng/mL; [4]<0.004 ng/mL

Table 3. Medians of PBDE congeners (ng/g lipid) found in umbilical cord blood serum from previous studies.

Study population	N	Year of sampling	BDE 47	BDE 99	BDE100	BDE153	BDE183	ΣPBDEs[a]	Reference
Madrid (Spain)	44	2003-2004	3.3	4.3	2.3	0.53	1.3	17	18
Sweden	15	2000-2001	0.98	0.07	0.07	0.17	0.01	1.69	31
Groningen (Netherlands)	69	2001-2002	0.5	0.1	0.1	0.9	na	3.9	30
Tolouse (France)	91	2004-2006	nd	7.4	1.4	0.48	0.59	12.3	27
Indiana (United States)	12	2001	25	7.7	4.1	4.4	nd	39	33
Baltimore (United States)	297	2004-2005	13.3	4.3	2.3	2.6	0.9	26.6	32
Indiana (United States)	16	2003-2004	13	5.3	2.6	2.7	1.3	31	34
New York (United States)	210	2001	11.2	3.2	1.4	0.7	0.6	18.4	35
South China	21	2005	1.4	0.47	0.22	0.8	0.2	3.9	28
Japan	8	2005-2006	0.57	nd	0.18	0.36	nd	0.65	29
Singapore	41	2006	1.69	0.35	na	na	na	3.3	36
Copenhagen (Denmark)	51	2007	nd	nd	nd	0.5	nd	0.95	37
Guiyu (China)	102	2007	2.1	0.64	0.18	0.99	0.91	13.8	38

[a]reported according to the number of congeners analyzed by the authors; na: not analyzed; nd: not detected

Table 4. PCBs concentrations in cord blood serum from Menorca and Valencia.

Compounds	Mean(SD)	Median	Percentile 25	Percentile 95	Range	Mean(SD)	Median	Percentile 25	Percentile 95	Range
	Valencia (n = 172) ng/ml [ng/g lipid]					Menorca (n = 88) ng/ml [ng/g lipid]				
PCB 28	0.007(0.04) [3.2(15)]	nd [nd]	nd[1] [nd]	0.03 [17]	nd-0.29 [nd-130]	0.03(0.12) [11(42)]	nd [nd]	nd[4] [nd]	0.24 [94]	nd-0.91 [nd-350]
PCB 52	0.005(0.02) [2.4(10)]	nd [nd]	nd[2] [nd]	0.04 [25]	nd-0.12 [nd-65]	0.05(0.14) [20(55)]	nd [nd]	nd[4] [nd]	0.28 [110]	nd-0.96 [nd-370]
PCB 101	0.008(0.02) [3.4(11)]	nd [nd]	nd[3] [nd]	0.06 [26]	nd-0.18 [nd-80]	0.06(0.19) [21 (71)]	nd [nd]	nd[4] [nd]	0.20 [93]	nd-1.6 [nd-610]
PCB 118	0.09(0.13) [35(45)]	0.067 [26]	0.03 [13]	0.22 [99]	nd-1.4 [nd-420]	0.10(0.13) [37 (51)]	0.08 [29]	nd[5] [nd]	0.30 [130]	nd-1.0 [nd-400]
PCB 138	0.12(0.16) [47(66)]	0.09 [35]	0.06 [23]	0.24 [110]	nd-1.8 [nd-640]	0.21(0.23) [80 (90)]	0.16 [60]	0.066 [25]	0.58 [260]	nd-1.5 [nd-560]
PCB 153	0.12(0.10) [50(45)]	0.11 [45]	0.08 [29]	0.23 [99]	nd-1.1 [nd-490]	0.27(0.48) [100(180)]	0.17 [66]	0.10 [38]	0.74 [310]	nd-4.3 [nd-1700]
PCB 180	0.10(0.07) [39(34)]	0.086 [35]	0.06 [24]	0.19 [77]	nd-0.76 [nd-350]	0.33(0.65) [130(250)]	0.12 [47]	0.081 [25]	1.8 [220]	nd-3.5 [nd-560]
ΣPCBs[b]	0.45(0.34) [180(150)]	0.38 [150]	0.27 [100]	0.89 [400]	nd-3.2 [nd-1500]	1.1(1.4) [400(520)]	0.65 [240]	0.28 [100]	3.2 [1200]	nd-10 [nd-4000]

[a]Arithmetic mean (standard deviation);[b] Sum of PCB congeners analyzed individually; nd: below limit of detection: [1]<0.07 ng/mL; [2]<0.06 ng/mL; [3]<0.03 ng/mL; [4]<0.005 ng/mL; [5]<0.02 ng/mL

Table 5. Arithmetic mean concentrations of OCs in umbilical cord blood serum reported in previous studies.

Area of study	N	Period of delivery	ΣPCBs[a,b] ng/ml [ng/g lipid]	HCB[a] ng/ml [ng/g lipid]	β-HCH[a] ng/ml [ng/g lipid]	4,4'-DDE[a] ng/ml [ng/glipid]	4,4´-DDT[a] ng/ml [ng/g lipid]	Reference
Ribera d'Ebre (Catalonia, Spain)	69	1997-1999	0.36[b]	1.1[b]	0.26[b]	0.83[b]	0.05[b]	10
Brescia (Italy)	70	2006	0.23[b]	0.05[b]	na	0.25[b]	nd	39
Rotterdam (Netherlands)	382	1990-1992	0.45	na	na	na	na	43
North Netherlands	51	1998-2000	[345]	na	na	na	na	44
Flanders (Belgium)	1054	2002-2003	[108]	[25.4]	na	[164]	na	42
Michalovce (Slovakia)	92	2002-2004	1.21	na	na	na	na	45
Wielkopolska (Poland)	17	2004	[65.5]	[21]	[2.6]	[365]	[19.6]	46
Sweeden	15	2000-2001	[104][c]	na	na	na	na	31
Faroe Island (Denmark)	316	1986-1987	[155]	na	na	[110]	na	47
Chukotka (Russia)	48	2001-2002	1.5	0.69	0.8	0.89	na	48
Northern Québec (Canada)	98	1995-2001	[350]	[55.6]	na	[387]	[16]	49
Québec (Canada)	656	1993-1995	0.51[b]	0.04[b]	na	0.41[b]	na	50
Artic Canada	407	1994-1999	0.36	0.10	0.07	0.53	0.03	51
Maryland (United States)	297	2004-2005	[16.9][c]	na	na	[53.5][c]	na	32
Oaxaca (Mexico)	86	2000	na	na	na	7540[b]	2370[b]	41
Veracruz (Mexico)	60	1997-1998	na	0.8	0.7	6.0	0.8	52
Rio de Janeiro (Brasil)	10	1997-1998	na	0.13	0.54	0.76	nd	53
Chiba and Yamanashi (Japan)	32	2002-2003	[63.8]	[10.9]	[33.8]	[33]	nd	54
Zhejiang (China)	60	2005	[194][b]	[6.15][b]	[2.33][b]	[83][b]	na	55
New Delhi (India)	23	2006-2008	na	na	3.59	1.98	0.93	56
Singapore	41	2006	[38.2]	na	[85.4]	[402]	[34.5]	57

[a]the concentrations are reported in the same units as given in the referenced studies. [b]the concentrations are reported according to the number of congeners analyzed by the authors; na: not analyzed; nd: not detected;[b] geometric mean; [c]median;

Table 6. Organochlorine pesticides concentrations in cord blood serum from Menorca and Valencia.

Compound	Mean(SD)	Median	Percentile 25	Percentile 95	Range	Mean(SD)	Median	Percentile 25	Percentile 95	Range
	Valencia (n = 172) ng/ml [ng/g lipid]					Menorca (n = 88) ng/ml [ng/g lipid]				
HCB	0.33(0.53) [140(240)]	0.24 [96]	0.12 [47]	0.72 [310]	nd-4.9 [nd-2200]	0.83(1.1) [320(440)]	0.68 [260]	nd[3] [nd]	1.9 [750]	nd-9.8 [nd-3800]
β-HCH	0.1(0.097) [41(43)]	0.092 [35]	nd[1] [nd]	0.25 [110]	nd-0.70 [nd-320]	0.25(0.46) [98(180)]	0.19 [60]	nd[3] [nd]	1.2 [510]	nd-2.1 [nd-810]
4,4'-DDE	0.77(0.91) [310(400)]	0.53 [210]	0.32 [130]	1.8 [850]	0.09-7.4 [nd-3700]	1.4(1.3) [530(480)]	0.94 [360]	0.54 [210]	3.5 [1500]	0.064-6.3 [nd-2400]
4,4'-DDT	0.059(0.15) [24 (64)]	nd [nd]	nd[2] [nd]	0.23 [100]	nd-1.3 [nd-630]	1.2(1.9) [45(73)]	0.047 [18]	0.030 [11]	0.44 [180]	0.030-0.44 [nd-410]

[a]Arithmetic mean (standard deviation); nd: below limit of detection: [1]<0.008 ng/mL; [2]<0.009 ng/mL; [3]<0.01 ng/mL

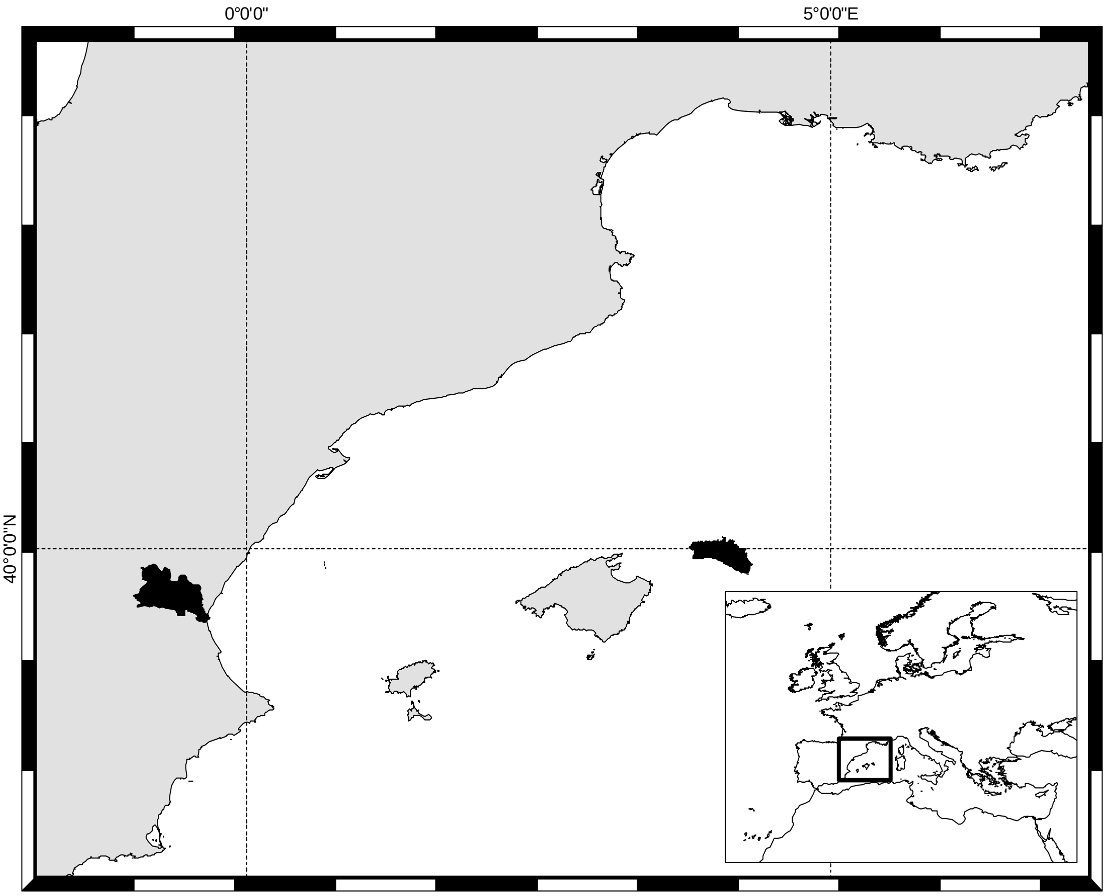
Figure Captions

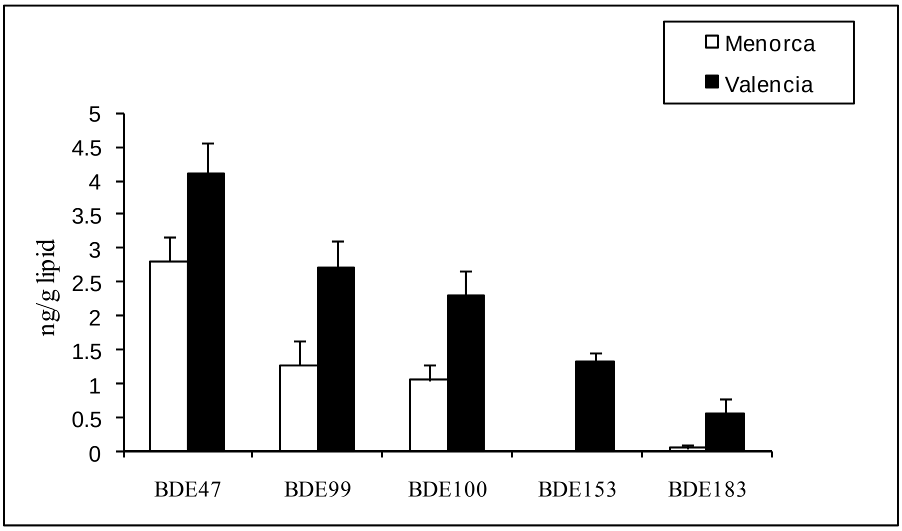
Figure 1. Areas of study

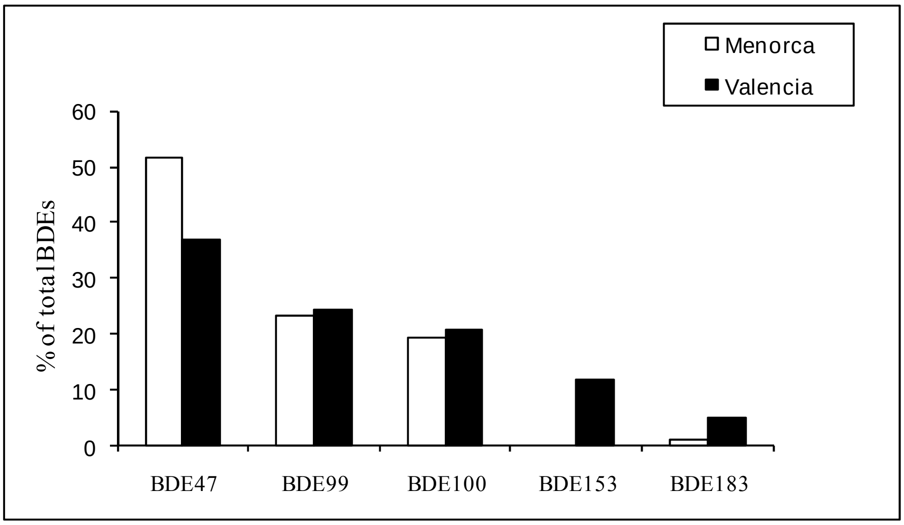
Figure 2. Mean concentrations (ng/g lipid) and standard error bars of the PBDE congeners (a) and contribution of the different individual congeners to the total Sum of BDEs (b) in Valencia and Menorca cord serum samples

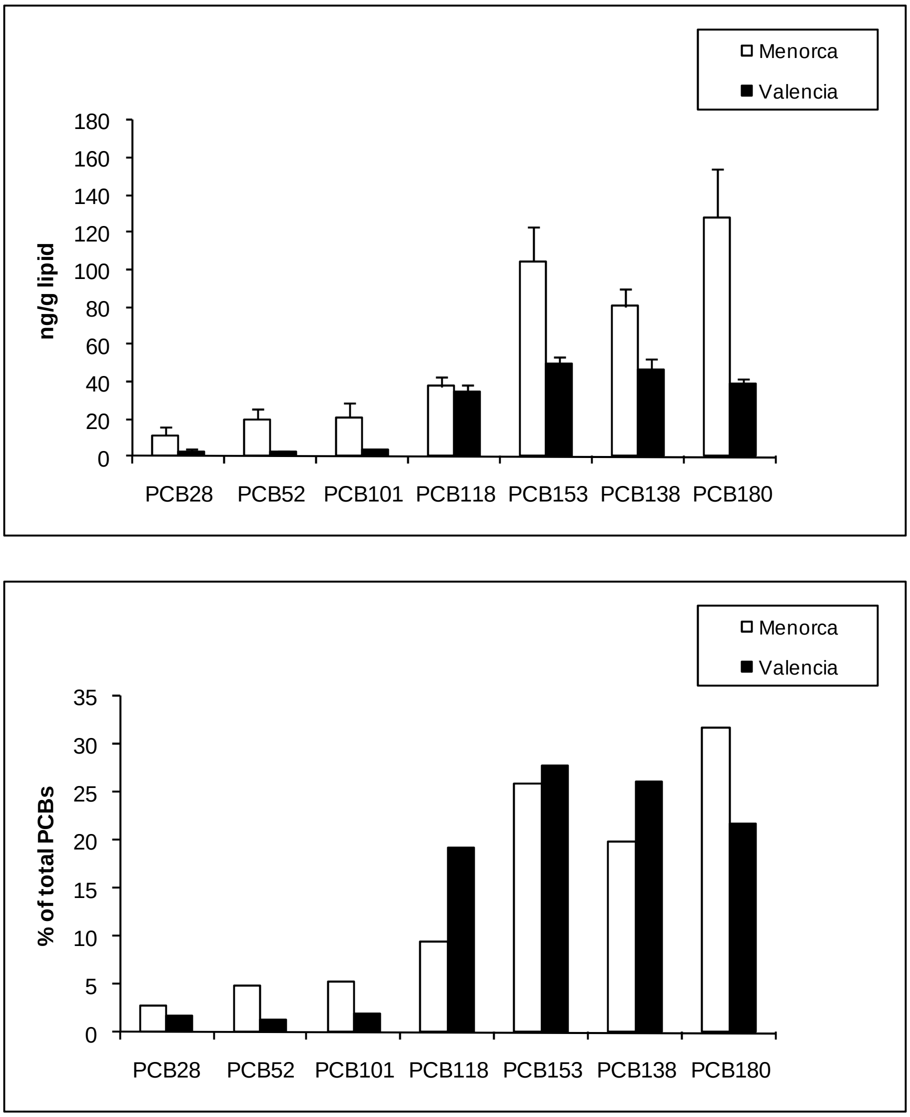
Figure 3. Mean concentrations (ng/g lipid) and standard error bars of the PCB congeners (a) and contribution of the different individual congeners to the total Sum of PCBs (b) in Valencia and Menorca cord serum samples

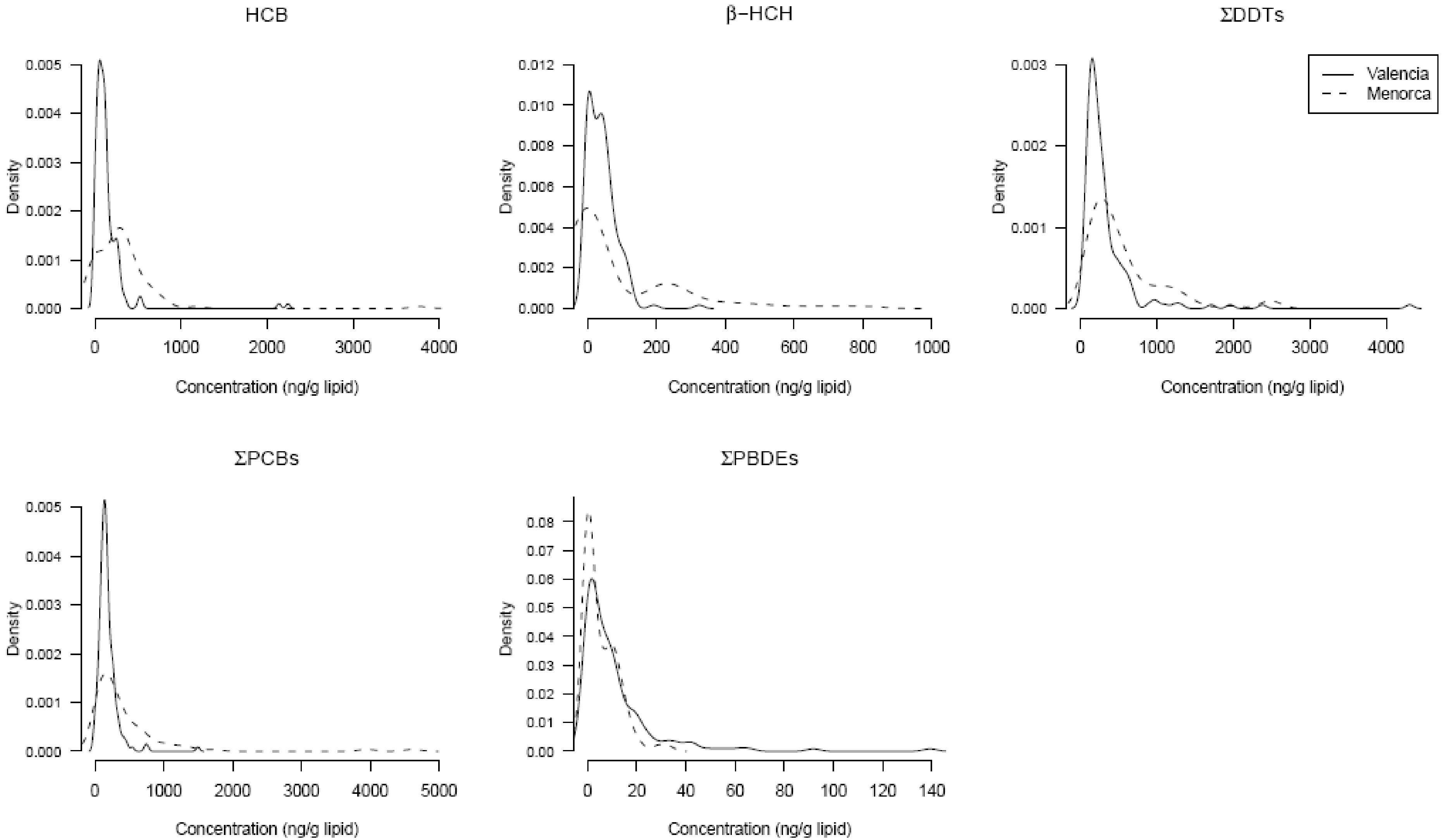
Figure 4. Frequency histograms showing the distribution of organohalogen compounds in cord blood serum from the cohorts of Valencia and Menorca.


0°0'0"
5°0'0"E
40°0'0"N


Menorca
Valencia
ng/g lipid
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
BDE47
BDE99
BDE100
BDE153
BDE183


Menorca
Valencia
% of total BDEs
60
50
40
30
20
10
0
BDE47
BDE99
BDE100
BDE153
BDE183


Menorca
Valencia
ng/g lipid
0
20
40
60
80
100
120
140
160
180
PCB28
PCB52
PCB101
PCB118
PCB153
PCB138
PCB180
Menorca
Valencia
% of total PCBs
0
5
10
15
20
25
30
35
PCB28
PCB52
PCB101
PCB118
PCB153
PCB138
PCB180


HCB
β−HCH
ΣDDTs
ΣPCBs
ΣPBDEs
Valencia
Menorca
Density
Concentration (ng/g lipid)